

# **How Does the Uptake of Gas Phase and Particulate Phase Smoke Constituents Relate to Cigarette Design ?**

## **The "Total Exposure" Project**

**Discussion Presentation Prepared by Philip Morris USA for the Institute of Medicine Panel Presentation 3/01/00**

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## Machine Cigarette Smoking Compared to Consumer Smoking

- Machine smoking
  - » Standardized method useful to assure consistency in manufacturing and inter-company comparison (e.g. FTC, ISO)
  - » Can provide relative ranking of smoke constituent yields
- Consumer smoking
  - » Individual smoking styles
    - › e.g. puff volume, frequency, duration
  - » Need biomarker measurements of uptake

## Rosa, et al., 1992

- 125 smokers who had smoked preferred brand for >24 weeks (approx. 11 cig./d) in 4 cigarette 'tar'/nicotine groups
- Serum cotinine measured 8 h after last cigarette (HPLC)

Rosa, M., Pacifici, R., Allieri, I., Pichini, S., Ottaviani, G., Zucarro, P., How the steady-state cotinine concentration in cigarette smokers is directly related to nicotine intake, Clin. Pharm. Ther., 52: 324-329 (1992)

# Results from Rosa, et al., 1992

VOLUME 32  
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Nicotine intake and cotinine levels 327

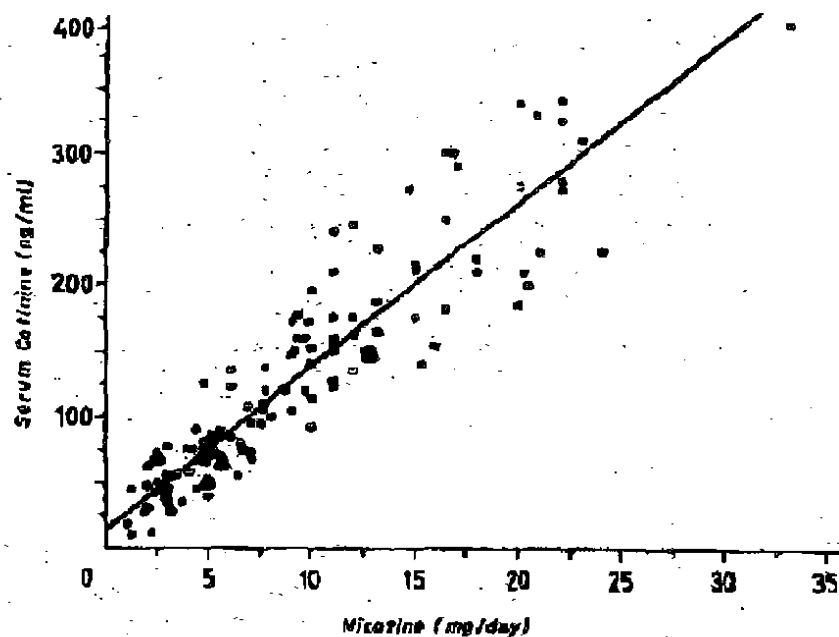


Fig. 2. Relationship between serum steady-state concentration of cotinine and daily available nicotine ( $n = 125$ ,  $y = 16.31 + 12.34x$ ,  $r = 0.919$ ,  $p < 0.0001$ ).

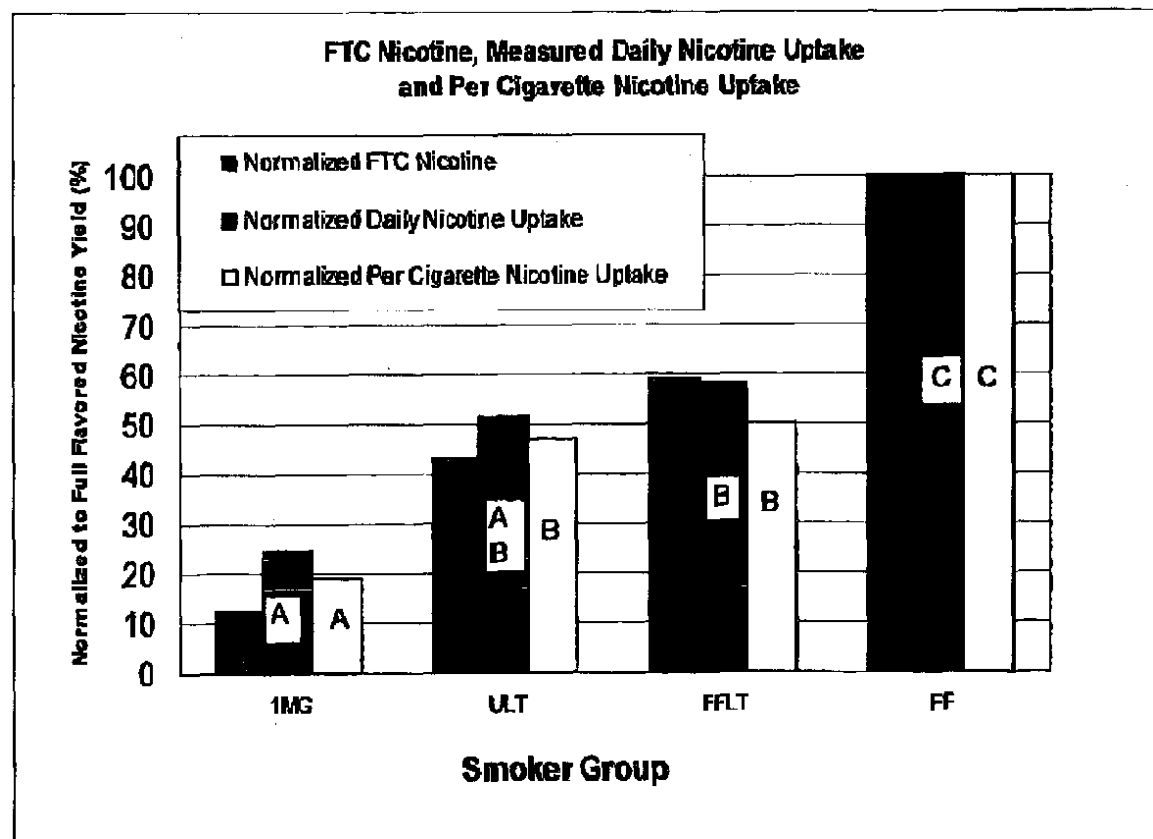
## Byrd, et al., 1995

- 33 smokers of their preferred brand (approx. 35 cig./d) in 4 cigarette 'tar' groups
- Urinary nicotine, cotinine, 3-OH-cotinine, and their glucuronide conjugates, and nicotine-N'-oxide\*, cotinine-N-oxide\*, demethylcotinine \* measured in 24-h samples (LC/GC-MS)

Byrd, G. D., Robinson, J. H., Caldwell, W. S., deBethizy, J. D. Comparison of measured and FTC-predicted nicotine uptake in smokers, *Psychopharmacology* 122: 95-103 (1995).

\* Not determined for the smokers of 1MG cigarettes.

# Data Extracted from Byrd (1995)

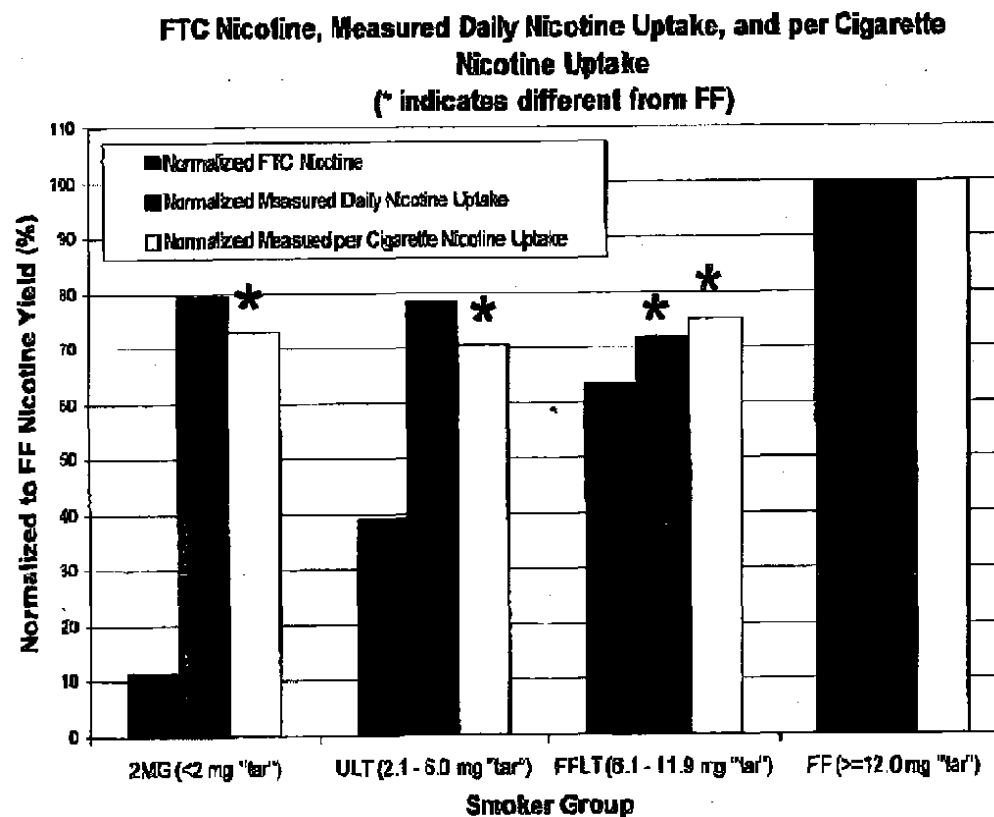


## Byrd, et al., 1998

- 72 smokers who had smoked their preferred brand >6 months (approx. 33 cig./d) in 4 cigarette 'tar'/nicotine groups
- Urinary nicotine, cotinine, 3-OH-cotinine, nicotine-N'-oxide, cotinine-N-oxide, demethylcotinine measured in three 24-h samples (LC-MS); salivary cotinine prior to last meal of day (RIA)

Byrd, G. D., Davis, R.A., Caldwell, W. S., Robinson, J. H., deBethizy, J. D., A further study of FTC yield and nicotine absorption in smokers, *Psychopharmacology* 139: 291-299 (1998)

# Data Extracted from Byrd (1998)



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# Summary of Results

- Results from population studies are not consistent between studies, even within the same laboratory
- Results from "switching" studies provide information on transient changes
- Various biomarkers have been used
- A majority of population studies have used nicotine and/or its metabolites
- These studies can be used as guides or pilots for the design of future studies

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# Biomarker Challenges

- Challenges for biomarkers
  - » uniqueness for tobacco smoke
  - » representation of particulate and gas phase
  - » representation of health-relevant constituents
  - » understanding of constituent metabolism
  - » concentration reflects uptake of cigarette smoke constituent(s)
  - » based on NRC guidelines of 1986

Benowitz, N.L., Biomarkers of environmental tobacco smoke exposure, Environmental Health Perspectives, 107(2): 349-355 (1999)

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# Potential Improvements

- Potential improvements in experimental design include
  - » smoke constituent, biomarker and biologic medium studied
  - » size and diversity of smoker population
    - › Geographic, Ethnic, Age, Gender demographics
    - › sufficient number of participants to ensure statistical power
  - » smoker compliance with test procedures
  - » collect information that could be useful to address relevant genetic polymorphism

# **Goal of Proposed "Total Exposure" Project**

**Using biomarkers determine the uptake of vapor phase and particulate smoke constituents for smokers of cigarettes with a range of yields of these constituents to provide a baseline for future cigarette-design related studies.**

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## Definition of "Total Exposure"

- Addresses both number and type of cigarettes smoked
- Include both particulate phase (PP) and gas/vapor phase (VP) constituents
- Exposure defined as average daily uptake in a 'steady state' situation
- Includes exposure to mainstream smoke, ETS, and other sources

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## Steps

- Determine smoke constituents and biomarkers to use
  - » Opportunity for input from health science community
- Identify validated analytical methods for measuring smoker exposure
  - » Opportunity for suggestions or information on newly developed methods
- Predetermine the criteria for measures of significance
- Determine relationship between cigarette parameters and total exposure

## Required Ancillary Information

- Number of cigarettes smoked/day
- FTC tar and nicotine rating of cigarettes smoked
- Diary/questionnaire information on how test population smokes
- Use objective measures wherever possible to supplement subject information

# Sampling and Analysis Methodologies

- No impact on subject smoking patterns
- High level of subject compliance
- Accepted and validated analytical methodology
- Establishment of analytical and biological variation (inter-personal, intra-personal)
- Data analysis with predetermined methods and research hypotheses

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## **Collaboration Opportunity**

- **What can Philip Morris contribute to this study**
  - » Knowledge of cigarette construction and testing
  - » Expertise in smoke composition and analysis
- **What can other experts contribute to this study?**
  - » Input on identification and aid to prioritize health-relevant smoke constituents and their biomarkers
    - › especially gas/vapor phase components
  - » population study methodologies

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## SUMMARY

The "*Total Exposure Project*" will contribute to improved understanding of the exposure of smokers to cigarette smoke constituents and establish a baseline for monitoring the impact of new cigarette designs on smokers' exposure.

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